UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/601,378	06/23/2003	David Farrow	SMB-004	7906

22463 7590 09/22/2009

SMART & BIGGAR
438 UNIVERSITY AVENUE
SUITE 1500, BOX 111
TORONTO, ON M5G 2K8
CANADA

EXAMINER	
SKOWRONEK, KARLHEINZ R	
ART UNIT	PAPER NUMBER
1631	

MAIL DATE	DELIVERY MODE
09/22/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

UNITED STATES PATENT AND TRADEMARK OFFICE

Commissioner for Patents
United States Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450
www.uspto.gov

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/601,378
Filing Date: June 23, 2003
Appellant(s): FARROW, DAVID

Matthew Zischka
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 15 July 2009 appealing from the Office action mailed 21 May 2008.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is incorrect. A correct statement of the status of the claims is as follows:

This appeal involves claims 1-5, 7, 8, and 22-29.

Claims 6 and 9-21 have been canceled.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

PAT 6391657	Bernhardt et al.	5-2002
PG PUB 2002/0042125	Petersen et al.	4-2002
PG PUB 2004/0072278	Chou et al.	4-2004

Tullis et al. ("HIV affinity hemodialysis as a treatment for AIDS", American Clinical Laboratory, p.22-23, October/November 2001)

Piesold (WO 01/85341, IDS entry B1, IDS filed 07 November 2005)

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 7, 8, and 22-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tullis et al. in view of Bernhardt et al., in view of Peterson et al., and in view of Piesold.

The claims are drawn to a method of detecting the presence of an analyte particle, the particle being a virus, specifically Human Immunodeficiency Virus (HIV), in a biological fluid, specifically blood. The method comprises the steps of filtering particulates that are larger than the virus into a first chamber and the virus particulates smaller than the virus in a second chamber, reacting the virus with a reagent to produce a complex that is larger than the virus alone in the second chamber, filtering the virus-reagent complex to remove particles that are smaller from the second chamber, and testing for the presence of the virus in the second chamber. In some embodiments, the reagents is truncated CD4. In some embodiments, filtering is done using injection molded plastic.

Tullis et al. teach a method of filtering HIV from blood using a filter that separates the cells (particles larger than the virus) from the HIV (p. 22, col. 1, para. 3, lines 7-10 to col. 2, line 1). Virus is passed through the filter where it complexes with a ligand reagent (antibodies) reactive to gp120 (p. 22, col. 2, lines 8-11) to allow further passage of particles smaller than the viral-reagent complex particles. Tullis et al. teach the detection of Viral-reagent complexes by PCR (col.1, para. 3, lines 10-14).

Tullis et al. does not show injection molded plastic and a CD4 reagent.

Bernhardt et al. teach the formation of virus-ligand complexes composed of CD4 receptor-HIV (table 1) to result in an increased particle size (col. 2, lines 10-18). The fluid containing the virus-reagent complex is subjected to ultrafiltration thereby allowing particles smaller than the virus-reagent complex to flow through the filter (col. 2, lines 20-29). Bernhardt et al. show that the method will increase the safety of plasma proteins

produced from human plasma for therapy and prophylaxis and will allow for an increased rate of filtration (col. 1, line 10-33).

Piesold describes a microfluidics device having a first chamber and a second chamber used in the filtration of analyte-reagent complexes. Piesold shows the device in figure 2. Piesold shows the device comprises a first chamber "waste", element 18, and a second "reaction" chamber, element 10. Piesold shows the reagent "beads" in the "reaction" chamber. Piesold shows that the reaction chamber is arranged to correspond in shape to a reaction detection/monitoring means (p. 3, lines 27-28). Piesold shows the device is applied in an example to perform a sequencing-by-synthesis technique in which nucleic acids labeled with biotin are made larger by binding to strepavidin-coated beads (p. 13, lines 2-12). Although Piesold shows the use of the device as applied to bead based assays, Piesold suggests that the device is also applicable to assays not involving beads, such as cell-cell separations, cell deformability tests, and particle filtration (p. 2, lines 31-32 to p. 2, lines 1-3). Piesold shows the device provides a reaction apparatus comprising a porous reaction chamber for trapping one or more particles therein and a reaction monitoring means arranged to monitor the particles trapped in the reaction chamber (p. 3, lines 24-28). Piesold shows that the device is shaped to conform to the shape of a reaction chamber-monitoring device (p. 3, lines 14-15). Piesold et al. shows the microfluidics device is sealed to allow the optical detection of the chemical reaction in the chamber (p. 12, lines 19-21). Piesold shows, in an example, a CCD camera is used to collect data from the device (p. 13, lines 20-21). Piesold suggests the device may be used to implement multi-step reactions at a single

location (p. 2, lines 18-19). The device of Piesold beneficially enhances the feasibility of miniaturizing many experiments, assays, etc (p. 2, line 5-16).

Peterson et al. show an injection molded plastic filtration device ([0011] and p. 9, claim 1). Peterson et al. teach the device has a solid support for capturing a desired analyte ([0050]). Peterson et al. show that the device has the superior blend of advantages of efficiency and convenience in design manufacture and use ([0010]).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the filter device of Tullis with the CD4 reagent of Bernhardt et al. because the binding of HIV to antibodies or to the CD4 protein are functionally equivalent. Bernhardt et al. show in table 1 that antibodies and CD4 are both suitable reagents for forming a reagent-HIV complex that may be retained during filtration of particles that are smaller than the reagent-virus complex. Bernhardt et al. further motivate one of skill in the art to modify the filter of Tullis et al. because Bernhardt et al. show that the method will increase the safety of plasma proteins produced from human plasma for therapy and prophylaxis and will allow for an increased rate of filtration. It would have been further obvious to modify the filter of Tullis et al. using the CD4 reagent of Bernhardt et al. with the microfluidics device of Piesold because Piesold shows the device provides a beneficial enhancement in the feasibility of miniaturizing experiments and assays. It would have been further obvious to modify the filter of Tullis et al. using the CD4 reagent of Bernhardt et al. with microfluidics device of Piesold because the application of differential filtering was known in the art at the time of invention as demonstrated by Tullis et al. and Bernhardt et al. One of

ordinary skill in the art would have been capable of applying differential filtering to the device of Piesold that was ready for improvement and the results would have predictable to one of ordinary skill in the art. It would have been further obvious to modify the filter device of Tullis using the CD4 reagent of Bernhardt et al. an the microfluidics device of Piesold with the injection molded plastic filtering device of Peterson et al. because Peterson et al. show that the device has the superior blend of advantages of efficiency and convenience in design manufacture and use.

Claims 1-5, 7, 8, and 22-29 rejected under 35 U.S.C. 103(a) as being unpatentable over Chou et al. in view of Bernhardt et al. and in view of Piesold.

The claims are drawn to a method of detecting the presence of an analyte particle, the particle being a virus, specifically Human Immunodeficiency Virus (HIV), in a biological fluid, specifically blood. The method comprises the steps of filtering particulates larger than the virus; reacting the virus with a reagent, producing a complex that is larger than the virus alone; filtering the virus-reagent complex, removing particles that are smaller; and testing for the presence of the virus. In some embodiments, the reagents is truncated CD4. In some embodiments, filtering is done using injection molded plastic.

Chou et al. shows a microfluidics system for particle analysis. Chou shows that viruses are manipulated and analyzed as particles with the microfluidics system ([0167]). Chou et al. shows the microfluidics device has size selective channels that

filter particles based on size ([0214]). In an embodiment, Chou et al. shows that blood is filtered with the device ([0460 and 0461]). Chou et al. shows that the device may be configured to have cascaded size selective combs that particles of different sizes are selected ([0468]). This reads on the limitation of the instantly claim invention of filtering out particle larger than the virus and smaller than the virus. Chou et al. teach that the input fluid may be composed of particle of heterogeneous sizes and that device has a size selective retention chambers ([0461]). Chou et al. shows the device is fabricated plastic using a mold ([0127 and 0132]). In example 15, Chou et al. shows that the microfluidics system is used as a diagnostic tool for analyzing heterogeneous populations of particles based on differences in size ([0655]). In that example, blood is introduced into the device where particles of the fluid are separated and are differentiated based on size. Chou shows that larger particles are retained where smaller particles pass through the size selective barrier ([0660]). Chou shows in example 15 that the particles are treated by exposure to a reagent ([0661]). Chou et al. shows the detection of reagent particle complexes. Chou et al. shows the microfluidics system has the advantages of improved speed, accuracy, safety, and cost ([0658]). Chou et al. shows that the CD4 receptor is the primary receptor for the human immunodeficiency virus (HIV) ([0701]).

Chou et al. do not show the formation of a reagent-particle complex that is separated from particles smaller than the complex; or a first chamber and a second reaction chamber separated by a filter.

Bernhardt et al. teach the formation of virus-ligand complexes composed of CD4 receptor-HIV (table 1) to result in an increased particle size (col. 2, lines 10-18). The fluid containing the virus-reagent complex is subjected to ultrafiltration thereby allowing particles smaller than the virus-reagent complex to flow through the filter (col. 2, lines 20-29). Bernhardt et al. show that the method will increase the safety of plasma proteins produced from human plasma for therapy and prophylaxis and will allow for an increased rate of filtration (col. 1, line 10-33).

Piesold describes a microfluidics device having a first chamber separated from a second chamber by a filter used in the filtration of analyte-reagent complexes. Piesold shows the device in figure 2. Piesold shows the device comprises a first chamber "waste", element 18, and a second "reaction" chamber, element 10. Piesold shows the reagent "beads" in the "reaction" chamber. Piesold shows that the reaction chamber is arranged to correspond in shape to a reaction-detection/monitoring means (p. 3, lines 27-28). Piesold shows the device is applied in an example to perform a sequencing-by-synthesis technique in which nucleic acids labeled with biotin are made larger by binding to strepavidin-coated beads (p. 13, lines 2-12). Although, Piesold shows the use of the device as applied to bead based assays, Piesold suggests that the device is also applicable to assays not involving beads, such as cell-cell separations, cell deformability tests, and particle filtration (p. 2, lines 31-32 to p. 2, lines 1-3). Piesold shows the device provides a reaction apparatus comprising a porous reaction chamber for trapping one or more particles therein and a reaction monitoring means arranged to monitor the particles trapped in the reaction chamber (p. 3, lines 24-28). Piesold shows that the

device is shaped to conform to the shape of a reaction chamber-monitoring device (p. 3, lines 14-15). Piesold et al. shows the microfluidics device is sealed to allow the optical detection of the chemical reaction in the chamber (p. 12, lines 19-21). Piesold shows in an example a CCD camera to collect data from the device (p. 13, lines 20-21). Piesold suggests the device may be used to implement multi-step reactions at a single location (p. 2, lines 18-19). The device of Piesold beneficially enhances the feasibility of miniaturizing many experiments assays, etc (p. 2, line 5-16).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the differential microfluidics particle filtering system of Chou et al. with the formation of CD4-HIV complexes for the purpose of increasing the HIV particle size of Bernhardt et al. because Bernhardt et al. show that by forming a reagent-particle complex increased filtration rates can be obtained. It would have been further obvious to use CD4 as the HIV complex-forming reagent because Chou et al. teach that CD4 is the primary receptor for HIV. It would also have been further obvious to modify the filtration device of Bernhardt et al. with the microfluidics system of Chou et al. because Chou et al. teach the microfluidics system has the advantages of improved speed, accuracy, safety, and cost. It would have been further obvious to modify the microfluidics filtering system of Chou et al. using the CD4 reagent of Bernhardt et al. with the microfluidics device of Piesold because Piesold shows the device provides a beneficial enhancement in the feasibility of miniaturizing experiments and assays. It would have been further obvious to modify the microfluidics filtering system of Chou et al. using the CD4 reagent of Bernhardt et al. with the microfluidics device design of

Piesold because the application of differential filtering was known in the art at the time of invention as demonstrated by Bernhardt et al. One of ordinary skill in the art would have been capable of applying differential filtering to the device of Piesold that was ready for improvement and the results would have predictable to one of ordinary skill in the art.

(10) Response to Argument

Regarding the rejection of claims 1-5, 7, 8, and 22-29 as unpatentable over Tullis et al. in view of Bernhardt et al. in view of Piesold and in view of Petersen under 35 USC 103 (a), appellant argues Tullis et al. in view of Bernhardt et al. in view of Piesold and in view of Petersen fail to show a testing for the presence of residual particles in a chamber in which a particle reagent complex is formed. The argument is not persuasive. Piesold shows an analyte-reagent complex is formed and trapped within a chamber (p. 3, line 24-26). Piesold shows the analyte-reagent complex is detected via a monitoring means arranged to monitor particles trapped in the reaction chamber (p. 3, line 26-27).

Appellant argues that Tullis et al. in view of Berhardt et al. in view of Piesold and in view of Petersen et al. does not suggest a second filtering to retain a residue of an analyte-reagent complex. The argument is not persuasive. Tullis et al. shows a filtering step in which particles, such as cells, larger than an analyte of interest are excluded from passing through submicron pores in the walls of hollow fibers in hemodialyis filter (p. 22, col. 1, line 41- p. 22, col. 2, line 6). Tullis et al. shows the space surrounding the fibers or “extra fiber space” is filled with a matrix comprising beaded agarose with

covalently attached anti-viral antibodies (p. 22, col. 2, line 3-6). The interaction of the viral particle with the beaded agarose with covalently attached anti-viral antibodies results in the formation of an analyte-reagent complex that is larger than the selected pore size of the filter. Thus, two filtering steps are employed in the hemodialysis filter of Tullis et al. Bernhardt et al. shows that by increasing the size of viral particles or analytes by incubation with a high molecular weight, ligand or reagent separation may be improved and a larger pore size selected, improving or increasing filtration rate (col. 1, line 6-14). Bernhardt et al. shows that a filter can be selected such that a particle smaller than the reagent-analyte complex can flow past. Piesold shows, as set forth above, an analyte-reagent complex can be formed and trapped within a chamber. Petersen et al. shows that a second chamber may be a reaction chamber formed in a separate reaction vessel coupled to the cartridge to receive the eluted analyte for further processing [0015].

Appellant argues Tullis et al. fails to disclose testing in a second chamber. The argument is not persuasive. Piesold et al. shows that the detection of analyte-reagent complex is detected in a chamber as set forth above. Appellant argues that the residue formed in the hemodialysis filter of Tullis et al. must be extracted from the hemodialysis device, however the claim recites the detection within the second chamber. The testing step of claim 1 is broad insofar as it can be interpreted as applicant has argued to mean *in situ* testing, or testing within the device and as taught by Piesold. Alternatively, the step of testing can also be interpreted as meaning *ex situ* testing as taught by Tullis et al.

Appellant argues that there is no reason a skilled person would be motivated to combine Tullis, Bernhardt, Piesold, and Petersen. The argument is not persuasive. In response to appellant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Tullis, Bernhardt, Piesold, and Petersen are all directed to purifying, isolating or sequestering biological samples. Since Tullis et al. does describe the detection or testing of analyte residue after filtration by increasing the size of the analyte virus, Petersen et al. provides the motivation for producing filtration device with injection molded plastic, Piesold et al. provides the motivation for miniaturizing experiments and assays, and Bernhardt et al. provides motivation for increasing the size of the analyte capture reagent.

Appellant's arguments for claims 22-25 and claims 26-29 reiterates the reasoning articulated form claim 1-5, 7, and 8. The arguments are not persuasive for the reasons provided above. The rejection is maintained.

Regarding the rejection of claims 1-5, 7, 8, and 22-29 as unpatentable over Chou et al. in view of Bernhardt et al. and in view of Piesold under 35 USC 103(a), Appellant argues Chou et al. does not show contacting an analyte particle with a reagent to form a

complex prior to further filtration steps. The argument is not persuasive because Bernhardt et al. shows an analyte particle with a reagent form a complex prior to further filtration steps (col. 1, line 6-14).

Appellant argues that Chou et al. does not suggest testing for the presence of analyte-reagent complex. The argument is not persuasive. Piesold shows an analyte-reagent complex is formed and trapped within a chamber (p. 3, line 24-26). Piesold shows the analyte-reagent complex is detected via a monitoring means arranged to monitor particles trapped in the reaction chamber (p. 3, line 26-27).

Appellant argues that Chou et al. does not show using the presence of an analyte as indicator of the analytes presence in the original fluid. The argument is not persuasive because Chou et al. shows in example 15 the application of blood to the system and the isolation of an analyte, white blood cells, and subsequent analysis of the white blood cells. Chou et al. expands the description of example 15 in example 26 to show the determination of the presence of non-blood cells and the like in the original sample [0885].

In response to appellant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Chou et al. and

Piesold are both directed to microfluidics separations and detection, Piesold and Bernhardt et al. show the formation of analytes reagent complexed that are larger than a selected pore size, and Chou et al. and Bernhardt et al. show embodiments directed to the analysis of blood for particular analyte particles. With respect to microfluidics, Chou et al. teaches such scaled-down assays may use less sample and reagent, may be less labor intensive, and/or may be more informative than comparable macrofluidic assays (Abstract). Piesold teaches his device provides a beneficial enhancement in the feasibility of miniaturizing experiments and assays (p. 2, line 5-16). With respect to the analysis of blood, Chou et al. teaches such systems may facilitate analysis of patient samples with improved speed, accuracy, safety, and/or cost, among others [0658]. Bernhardt et al. teaches that increasing the size of viruses in blood increases the separation effect.

With respect to appellant's argument of no reasonable expectation of success, the argument is not persuasive as Berhardt et al. successfully shows the capture of viral particles by increasing the size of the vial particle via the formation of virus-reagent complex.

Appellant's arguments for claims 22-25 and claims 26-29 reiterates the reasoning articulated above for claims 1-5, 7, and 8. The arguments are not persuasive for the reasons provided above. The rejection is maintained.

In response to appellant's argument, at p. 32 of the brief, that the examiner has combined an excessive number of references, it is noted that reliance on a large number of references in a rejection does not, without more, weigh against the

obviousness of the claimed invention. See *In re Gorman*, 933 F.2d 982, 18 USPQ2d 1885 (Fed. Cir. 1991).

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/KARLHEINZ R SKOWRONEK/

Examiner, Art Unit 1631

Conferees:

/Marjorie Moran/

Supervisory Patent Examiner, Art Unit 1631

/Joseph T. Woitach/

Supervisory Patent Examiner, Art Unit 1633